DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
22215 26th Ave SE Suite 210 Bothell, WA 98021 (425) 302-0340 Fax:(425) 302-0404 Industry Information: www.fda.gov/oc/industry	08/04/2014 - 08/28/2014* FEI NUMBER 3005580627

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Denise S. Burnham, President and Owner

FIRM NAME	STREET ADDRESS
Oregon Compounding Centers, Inc. dba Creative Compounds	8560 Sw Salish Ln Ste 100
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Wilsonville, OR 97070-9625	Producer of Sterile Drug Products

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, and followed.

Specifically,

A. Aseptic Techniques observed on 08/04-05/14 were inadequate for the manufacturing of sterile injectable drug products as follows:

1. On 08/04/14 an operator wearing non-sterile gloves placed the non-sterile components and supplies in the ISO 5 hood for producing Alprostadil/Lidocaine without disinfecting the items. After putting on sterile gloves, the operator entered the ISO 5 hood, touched all of the non-sterile materials, removing their packaging and discarded the packaging in the ISO 5 hood next to where Alprostadil/Lidocaine 20mcg/10mg/mL Lot 20140801@15 was being sterile filtered and filled into a 5mL vial. There was no disinfection of gloves, area or equipment is conducted during these activities.

2. On 08/04/14 during the filling of Alprostadil/Lidocaine 20mcg/10mg/mL syringes, Lot 20140801@15 we observed the product leaking out of the syringe and filter. The operator had selected a filter incompatible with ethyl alcohol and went to the ISO 8 area to retrieve the correct filter. The operator did not perform any sanitization of gloves and did not disinfect the new filter prior to introducing the item into the ISO 5 hood.

3. The following issues were noted during the manufacturing of MSM 15% Injectable Lot 20140804@14 on 08/05/14 in the ISO 8 area and then moved to ISO 5 hood for the aseptic filling

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process.

a. The product was formulated in the ISO 8 prep room in a pre-sterilized beaker using non-sterile MSM powder.
b. During the mixing of MSM powder with sterile water for injection, the paperwork was observed lying on the top of the open beaker.
c. The operator used a syringe to check the pH of the formulated MSM 15% and poured the contents from the syringe back into the beaker after testing the pH.
d. In the ISO area, the operator formulating MSM 15% injectable was wearing non-sterile gloves and grabbed the open beaker from the top. This operator handed over the beaker to another operator who placed the beaker in the ISO 5 hood without disinfecting it.
e. During the aseptic filling of MSM 15% Injectable into 100 mL vials in the ISO 5 hood, the operator initially used a Repeater Pharmacy pump to fill vials using sterile single use tubing containing a 0.2 micron filter. After filling three vials, the product started leaking from the tubing. The operator poured the contents of three vials back into the beaker containing the formulated drug product for the Lot 20140804@14.

4. On 8/5/14 during the re-packaging of Avastin 1.25mg/ 0.05mL, Lot 20140805@1 into single use syringes in the ISO 5 hood, the operator withdrew Avastin into a 0.3 mL syringe from an opened and uncapped 4 mL (25mg/ mL) vial and dispensed any excess amount of the desired volume of 0.05 ml back into the 4 mL Avastin vial that was used to fill a batch of 80 syringes. No further sterility measures are performed on these repackaged syringes prior to their distribution.

5. Personnel were observed on 08/04-05/14 entering the ISO 8 prep room from the unclassified area without donning any gowning materials while performing production checks and interacting with gowned personnel.

B. There is no data to support the continued sterility of 30, 50 and 100mL vials that undergo in-house sterilization and depyrogenation. The vials are stored in the ISO 8 area on a shelf near the floor where people enter and exit the room wearing street clothes. The top of the vials are individually covered with aluminum foil from the sterilization cycle and are stored for up to 90 days until the time of use.

C. There is no data to support continued sterility of stoppers that undergo in-house sterilization in the Tuttnauer Autoclave. The stoppers are stored in the ISO 8 area wrapped in autoclave paper

in a bin on a shelf near the floor where people enter and exit the room wearing street clothes. The stoppers are labeled with a 90 day expiration date.

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include validation of the sterilization process.

Specifically,

A. SOP 7.7007.31,The High Risk Process Simulation Testing, does not specify all aseptic filling operations performed in the ISO 5 hood. The simulation test observed on 08/06/14 only simulates filling a 30mL syringe with an attached 0.2µ filter and transferring the product to 6 pre-sterilized and pre-depyrogenated, stoppered and capped 10mL vials with 10mL of media, as specified in your procedure. However, you also fill 1, 2, 5, 10, 30, 50 and 100mL vials sizes and have batch sizes ranging from 1 - 320 units.
   1. The 30, 50 and 100mL vials are not pre-sterilized and undergo sterilization and depyrogenation in-house and no media fill simulations have been conducted using this container/closure system.
   2. You conduct syringe-to-syringe transfers and filling, however you have not conducted any media fill simulations using this filling process.
   3. You fill pre-mixed bulk drug products from a beaker using a Repeater Pharmacy pump with tubing and syringe containing a 0.2m filter into open vials and you have not conducted any media fill simulations using this filling process.
   4. You conduct vial-to-syringe filling and have not conducted any media fill simulations using this filling process.
   5. You allow a maximum of three operators in the ISO 7 area that can perform aseptic processing in the ISO 5 hoods during production of sterile drug products. Your media fill simulations are for one operator at a time and no interventions or interruptions are simulated during your media fills

B. The moist heat sterilization process (autoclave) for stoppers or loading patterns and cycle times

used for terminal sterilization of aseptically filled drug products is not validated. You stated you use a Biological Indicator with each load to confirm sterility.

1. You stated that you autoclave stoppers for 20 minutes at 20 PSI and 250F. This is not documented;
2. For drug products no cycle parameters are documented on the Logged Formulation Worksheets. For example: Sodium Phosphate 92/93mg/mL Injectable, Calcium Gluconate 10% Injectable and Glycerin 72% v/v are terminally sterilized and there is no documentation on the Logged Formulation Worksheets of any of the autoclave parameters used.

C. The Millipore 0.2µ filter used in the vacuum filtration unit does not undergo any pre or post-use filter integrity testing. You use the vacuum filtration unit to sterile filter lots that are larger than 300mL, which includes sterile injectable products such as MSM 15% and Ascorbic Acid (preserved and preservative free) 500mg/mL.

D. There is a failure to validate the 0.2µ filters used to manufacture steriule injectable drug products produced from non-sterile components which includes Alprostadil, Bevacizumab/Dexamethasone, Glutathione 100mg/mL. In addition, no pre-filtration bioburden limits have been established in order to determine if it exceeds the maximum capabililty of the filter.

OBSERVATION 3

Written records are not made of investigations into the failure of a batch or any of its components to meet specifications.

Specifically,your firm did not investigate testing results that show drug products have failed to meet specifications for sterility. For example, Methylcobalamin 20mg/mL Lot 20140219@1/1 failed sterility testing on 02/24/14 and Glutathione 100mg/mL injectable (Preserved) Lot # 20140620@13 failed sterility testing on 06/25/14 and you have not performed any investigation or implemented any corrective actions regarding these failed results. You have not performed an impact assessment to other products produced in the ISO 5 hood during the same time frame.

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OBSERVATION 4

Each batch of drug product purporting to be sterile is not laboratory tested to determine conformance to such requirements.

Specifically,

A. Sterility testing is not always performed on each batch of finished sterile injectable drug product produced. For example, no sterility testing is performed on any batches that are terminally sterilized which includes: Calcium Gluconate 15% (Preservative Free) Injectable, Sodium Phosphate 93/93 mg/ml (Preservative Free) Injectable, and Selenium 200mcg/mL (Preservative Free). Sterility testing is not performed on batches of injectable drug products that are stored frozen for up to 45 days followed by 3-day refrigerated conditions which includes Alprostadil/Lidocaine 20mcg/10mg/mL

B. Endotoxin is not always performed on all batches of sterile injectable finished products. From January 2013 to August 2014 only 13 lots of finished sterile drug products were tested for endotoxin. Additionally, no endotoxin testing is performed on any non-sterile ingredients used in the manufacture of these drug products.

C. All of your finished sterile drug products samples are tested for sterility by a contract laboratory using a ScanRDI rapid sterility test method. No method suitability testing for the sterility test method was performed to ensure that the specific drug product samples tested do not interfere with the test.

OBSERVATION 5

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity and strength of each active ingredient prior to release.

Specifically, potency testing is performed on a skip-lot testing schedule that tests no more than 5% of any finished product lots. You do not test for potency of the final drug product after performing dilution steps as part of the manufacturing process for numerous sterile drug products. For example, the admixture process for Mitomycin 0.2mg/mL and 0.3mg/mL Injectable requires two complex dilution steps.

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OBSERVATION 6

Clothing of personnel engaged in the manufacturing and processing of drug products is not appropriate for the duties they perform.

Specifically,

A. The gowns worn by operators when working in the ISO 5 hood are not sterile and the surgical masks do not provide adequate coverage to the forehead, neck or face. Your procedure SOP 7.011 "Gowning and Gloving" allows for re-use of the gown during the production day to re-enter the ISO 5 and ISO 7 areas. On 08/04-05/14 we observed the operator store the mask and hairnet used while producing sterile drugs in the sleeve of her gown and re-used these items throughout the day. Additionally, an operator was observed wearing her personal tinted eyeglasses during filling of Avastin lot 20140805@1, which were not disinfected. 6.

B. On 08/05/14 during the repackaging of Avastin Lot 20140805@1 in the ISO 5 hood the operator's wrists were exposed due to inadequate glove and gown cover.

OBSERVATION 7

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically, your firm aseptically fills drug products in the ISO 5 Hoods and the ISO 7 and ISO 8 processing and support rooms and the procedure, SOP 9.038, "Surface Sampling Plan" for monitoring the areas are deficient in that:

A. Active air sampling for non-viable and viable monitoring is not performed each day in the ISO 5 hood when sterile drug products are produced. Instead it is performed every six months under static conditions.

B. Surface sampling for microbiological monitoring is not performed each day that a batch of sterile drug is filled. Instead it is conducted every two weeks in the ISO 5 hood and the ISO 7 and ISO 8 areas.

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Also the locations where samples are taken is not identified or documented.

C. Personnel monitoring of the operator's fingertips is not performed each day that a batch of sterile drug is filled in the ISO 5 hood. Instead the current procedure is to perform personnel monitoring every two weeks.

OBSERVATION 8

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically,
A. The suitability and efficacy of disinfectants, cleaning agents and procedures have not been assessed to ensure potential contaminants are adequately removed from the surfaces in the classified areas. Routine cleaning procedures for the ISO 5 hood include using 70% IPA as a disinfectant. Virustat DC Plus and Acidified Bleach are rotated quarterly as the cleaning agents. The concentration of the acidified bleach is not documented.

B. The wipes used to clean the ISO 5 hood and ISO 7 and ISO 8 support rooms are non-sterile, non-woven and have not been established as non-shedding.

OBSERVATION 9

Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure.

Specifically,
A. No static and dynamic airflow pattern studies (smoke studies) have been performed in the ISO 5 hood or ISO 7 buffer room where sterile injectable drug products are prepared and filled.

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B. There is no continuous monitoring of air pressure differentials from the ISO 7 room to the ISO 8 room. It was observed that opening the doors to the ISO 7/8 area affects the pressure differentials of these areas.

OBSERVATION 10

An adequate number of batches of each drug product are not tested to determine an appropriate expiration date.

Specifically, your firm does not have stability program or data to support Beyond Use Dates (BUD) assigned to sterile finished injectable drug products filled on site. No stability studies have been conducted to support assigned dates. For example:
Glutathione 100mg/mL, Preservative Free has a BUD of 90 days at refrigerated conditions
Glutathione 100mg/mL, Preserved, has a BUD of 120 days at refrigerated conditions
Methlycobalamin 20 mg/mL Preservative Free has a BUD of 180 days at refrigerated conditions

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*** DATES OF INSPECTION:**
08/04/2014(Mon), 08/05/2014(Tue), 08/06/2014(Wed), 08/07/2014(Thu), 08/08/2014(Fri), 08/11/2014(Mon), 08/12/2014(Tue), 08/13/2014(Wed), 08/27/2014(Wed), 08/28/2014(Thu)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."